Some Compounds Derived from Ethyl p-Diiminosuccinylo-succinate

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DISSERTATION

SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN THE FACULTY OF PURE SCIENCE OF COLUMBIA UNIVERSITY

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JOHN MAURICE NELSON, B.S.

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I take this opportunity to thank him for his valuable assistance and advice throughout this work, and also for the interest he has shown in its progress.

I also wish to express my thanks to Dr. K. G. Falk and Dr. V. J. Chambers for the many valuable suggestions they have offered.

J. M. NELSON.

Organic Chemical Laboratory, Havemeyer Hall,
Columbia University, May, 1907.

GENERAL INTRODUCTION.

This dissertation treats of ethyl diminosuccinylosuccinate and several compounds derived from it by some various chemical reactions. Although the mentioned ester has served as the starting material, throughout this work, the problems involved are essentially different, and therefore it was deemed advisable to present the subject in three parts:

I. Naphthotetrazines.

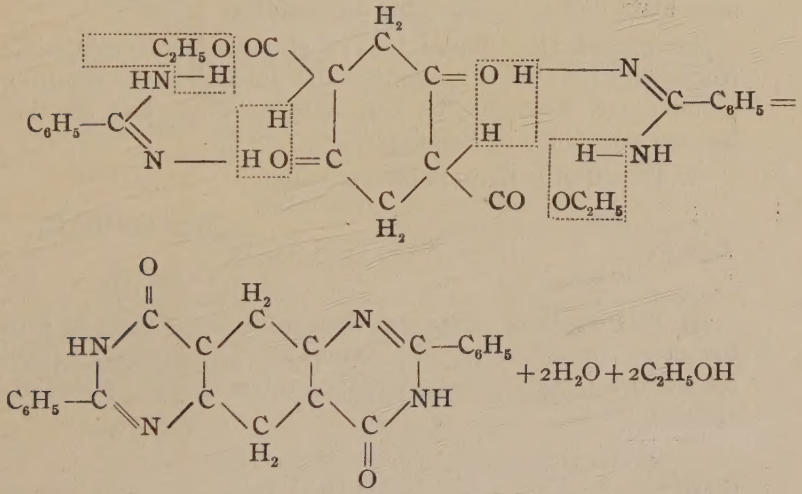
II. Isomerism of Ethyl *p*-Diiminosuccinylosuccinate and Ethyl *p*-diaminoterephthalate.

III. A Double Indigo.

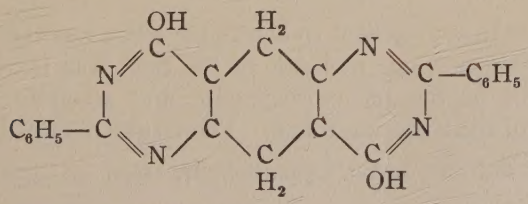
PART I.

NAPHTHOTETRAZINES.

In 1889 Pinner,[1] in connection with some work on the condensation of benzamidine with ketocarboxylic esters, obtained from benzamidine and ethyl succinylosuccinate a new three-ringed heterocycle to which he assigned the name dihydrodiphenyldioxyantetrazine. From the behavior of benzamidine towards ketocarboxylic esters in forming pyrimidine derivatives, Pinner represented the reaction taking place by the following equation:



and since the antetrazine reacted with alkalies in forming salts, he considered that it contained two enolic groups, and therefore the structure:



[1] Pinner, Ber., 22, 2609 (1889).

In extending the work upon the quinazolines Bogert and Dox[2] conducted some experiments with ethyl *p*-diaminoterephthalate in the hope of obtaining naphthotetrazines therefrom by the usual quinazoline condensations. These authors decided to use the name naphthotetrazine in place of antetrazine, since the former is more in accord with the nomenclature adopted by Richter's Lexikon for such heterocycles.

Their attempts proved unsuccessful in the case of ethyl *p*-diaminoterephthalate but they were finally successful in obtaining the naphthotetrazines through a method, independently, although similar to that of Pinner. In place of benzamidine, they carried out the condensations between ethyl succinylosuccinate and quanidine also acetamidine.

Bogert and Dox[3] found that ethyl *p*-diaminoterephthalate reacts with phenylisocyanate, but did not isolate the resulting product and determine its true nature. Since this reaction has the possibility of forming:

I. The ethyl *p*-diuraminoterephthalate,

$$C_6H_2\left(\begin{matrix}NH_2\\COOC_2H_5\end{matrix}\right)_2 + 2C_6H_5NCO = C_6H_2\left(\begin{matrix}NHCONHC_6H_5\\COOC_2H_5\end{matrix}\right)_2$$

II. This resulting compound then being acted upon in turn by more phenylisocyanate giving the 3,8,-diphenyl-2,4,7,9, tetraketo-1,3,7,8,-octahydronaphthotetrazine and phenylurethane,

$$C_6H_2\left(\begin{matrix}NHCONHC_6H_5\\COOC_2H_5\end{matrix}\right)_2 + 2C_6H_5NCO =$$

$$C_6H_2\left(\begin{matrix}NH-CO\\CO-N-C_6H_5\end{matrix}\right)_2 + 2C_6H_5NHCO_2C_2H_5$$

Therefore it was decided to determine what was the product formed, when first one molecule of the ester was treated with 2 molecules of the phenylisocyanate and secondly when 4 molecules of the latter was taken. The results obtained showed

[2] Bogert and Dox, J. Am. Chem. Soc., **27**, 1127.

[3] See **2**.

that reaction always took place even when phenylisocyanate was present in excess and not as indicated by (II).

Phenylisocyanate not being able to bring about the condensation of the diphenyluramino derivative into the corresponding naphthotetrazine, it was hoped that by using acetic anhydride, the condensation could be effected. Instead of this taking place, however, the phenyluramino groups were broken up, obtaining thereby the ethyl *s*-diacetyl-diaminoterephthalate. The reactions taking place can be expressed by the following equations:

$$C_6H_2\left(\begin{matrix}NHCONHC_6H_5\\COOC_2H_5\end{matrix}\right)_2 + 2(CH_3CO)_2O =$$
$$C_6H_2\left(\begin{matrix}NHCOCH_3\\COOC_2H_5\end{matrix}\right)_2 + 2C_6H_5NHCOCH_3 + CO_2$$

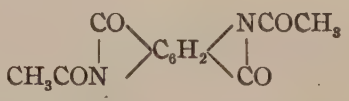
$$C_6H_2\left(\begin{matrix}NHCONHC_6H_5\\COOC_2H_5\end{matrix}\right)_2 + 4(CH_3CO)_2O =$$
$$C_6H_2\left(\begin{matrix}N(COCH_3)_2\\COOC_2H_5\end{matrix}\right)_2 + 2C_6H_5NHCOCH_3 + 2CO_2$$

It is worth noting that the ethyl tetraacetyldiaminoterephthalate was easily obtained by this reaction, whereas only the diacetyldiaminoterephthalate was formed by the action of acetic anhydride or acetyl chloride upon ethyl *p*-diaminoterephthalate itself. This suggests the possibility that other primary amines which yield only monacetyl derivatives by direct acetylation may be converted into the diacetyl derivatives through the phenyluramino compound.

Since the acetyl derivatives of ethyl *p*-diaminoterephthalate could be obtained by this procedure, it was decided to repeat more carefully the experiments of Bogert and Dox and see if the ester could not be acetylated directly by means of acetic anhydride. It was found that the acetylation did take place, yielding the ethyl *s*-diacetyl-diaminoterephthalate. Furthermore, the same product was obtained by means of acetyl chloride and the ester in presence of a base like calcium carbonate.

Meyer[4] has shown that bibasic acids condense with aromatic *p*-diamines, yielding acyl derivatives in which both of the hydrogens of the amino groups have been replaced by the acyl groups. By fusing ethyl *p*-diaminoterephthalate with phthalic anhydride, ethyl *p*-diphthalimidoterephthalate was obtained. This reaction was also tried with ethyl diiminosuccinylosuccinate, but the results were not satisfactory. Since ethyl *p*-diaminoterephthalate was found to be acetylated quite readily it seemed worth while to see what would be the behavior of ethyl diiminosuccinylosuccinate under similar treatment. The diimine derivative was found to acetylate by boiling with acetic anhydride, forming ethyl *s*-diacetyldiiminosuccinylosuccinate. The yield in this case was, however, not as good as in the case of ethyl *s*-diacetyl-*p*-diaminoterephthalate prepared in the same way, due to more decomposition. It was also found that by treating ethyl diiminosuccinylosuccinate with acetyl chloride or with benzoyl chloride in the presence of pyridine that the acylation took place, yielding the diacyl derivatives. By adding bromine to an acetic acid solution of the benzoyl derivative, oxidation apparently took place, as a product was obtained, having a higher melting point, and was very likely ethyl *s*-dibenzoyl-*p*-diaminoterephthalate.

Next *p*-diaminoterephthalic acid was boiled with acetic anhydride to see whether it would also be acetylated as in the case of its ester, forming the corresponding diacetyl derivatives or the diacet-dianthranil, or whether no reaction would take place as stated by Bogert and Dox. The resulting product was found to be the diacet-dianthranil (dilactam of *s*-diacetyl-*p*-diaminoterephthalic acid.

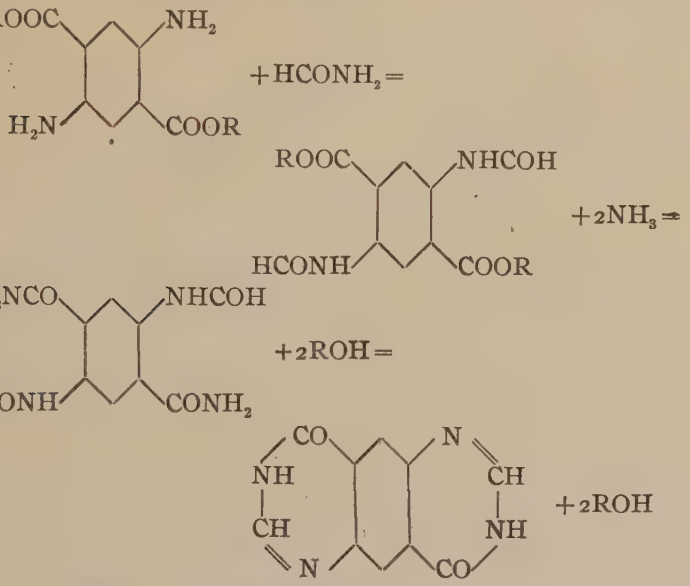


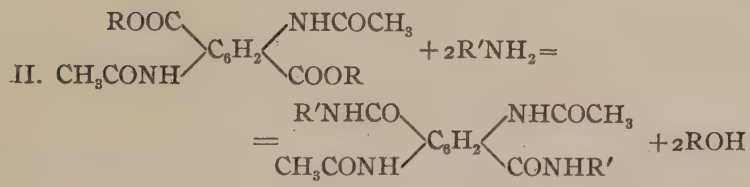
Naphthotetrazines were prepared by heating ethyl *p*-diaminoterephthalate with formamide (I)[5] by heating its acetyl

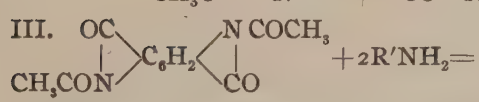
[4] Meyer, Ann. der Chem., **347**, 17.

[5] Niementowski, J. prakt. Chem. [2], **51**, 564 (1895); Bogert and Chambers, J. Am. Chem. Soc., **27**, 650.

derivative with primary amines (II)[6] by the action of primary amines upon the above diacetdianthranil (III)[7] and by heating the diphenyluraminoterephthalate with aniline (IV), the reactions involved being as follows:

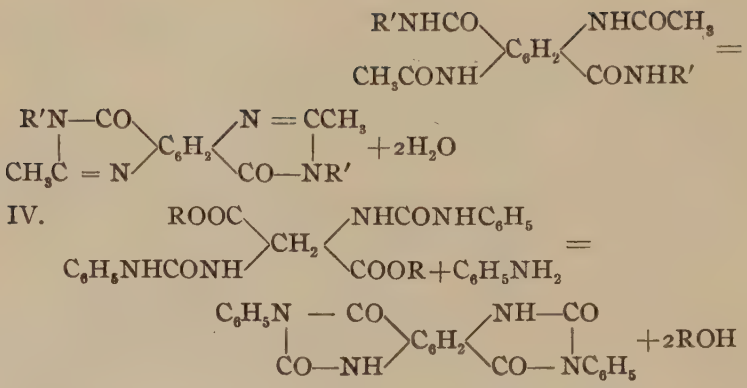
I. 

II. 

III. 

[6] Weddige, J. prakt. Chem. [2], **36**, 141 (1887); Zacharias, *Ibid.*, **43**, 432 (1891); Thieme, *Ibid.*, **43**, 451 (1891).

[7] Anschütz, Schmidt and Greiffenberg, Ber. **35**, 3480 (1902); Bogert and Chambers, J. Am. Chem. Soc., **27**, 649 (1905); Bogert and Seil, *Ibid.*, **27**, 1305 (1905); *Ibid.*, **28**, 884 (1906).



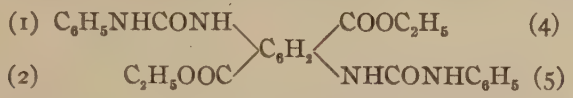
By these various reactions, the following naphthotetrazines were prepared: 4,9-diketotetrahydro-1,3,6,8-naphthotetrazines, (4,9-dihydroxy-1,3,6,8-naphthotetrazine), the 2,7-dimethyl derivatives of the latter, 2,7-dimethyl-3,8-diisoamyl-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine (and corresponding intermediate amide), 2,7-dimethyl-3,8-diphenyl-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine, and 3,8-diphenyl-2,4,7,9-tetraketo-octahydro-1,3,6,8-naphthotetrazine (3,8-diphenyl-2,7-dihydroxy-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine). Most of these substances melt very high or are infusible. They are insoluble or very difficultly soluble in the usual organic solvents. The isoamyl compound, however, melts relatively low (179°corr.) and can be crystallized from alcohol. Of the naphthotetrazines investigated so far, those containing the group —CONH—C(OH):N— dissolve readily in dilute alkalies and are reprecipitated by dilute acids or by carbon dioxide.

EXPERIMENTAL PART.

The preparation of *p*-diaminoterephthalic acid was carried out as described by Bogert and Dox[8] by converting ethyl succinylosuccinate into its diimine, oxidizing this to ethyl diaminoterephthalate, and saponifying the latter. In the oxidation of the diimine to the diamino ester by the action of bromine and sulphuric acid, the observation was made that the diimine must be added to the acid, and not the acid to the

[8] Bogert and Dox, J. Am. Chem. Soc., 27, 1136 (1905).

diimine. If the latter order is followed, sufficient heat is generated to destroy much of the diimine, unless recourse is had to external cooling. *Ethyl Diphenyluraminoterephthalate*,

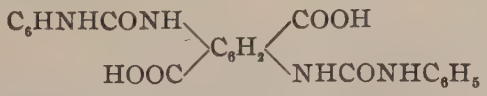


Three grams (one molecule) of ethyl diaminoterephthalate were dissolved in 60 cc. of dry benzene in a flask provided with a return condenser and placed on the steam bath, and 2.83 grams (two molecules) of phenylisocyanate added to the clear solution (excess of phenyl isocyanate did not effect the results). After warming for a few minutes the phenyluramino derivative began to separate as a light yellow precipitate, and in about fifteen minutes the reaction was complete, the yield being practically theoretical. The precipitate was filtered and washed with dry benzene, recrystallized from nitrobenzene, washed well with hot alcohol, dried at 110° to constant weight, and analyzed with the following results: Found: C, 63, 22; H, 5.24; N, 11.19. Calc. for $C_{26}H_{26}O_6N_4$: C, 63.93; H, 4.91; N, 11.47.

On account of the insolubility of this substance it is difficult to thoroughly purify it, and this is the cause of the somewhat wide variation of the percentage found from those calculated.

The pure phenyluramino compound is a light yellow, crystalline solid, melting with decomposition at about 262°. It is very difficultly soluble in water, alcohol, carbon tetrachloride, ethyl acetate, amyl valerate or benzene, but may be crystallized from nitrobenzene. Acetic anhydride gradually dissolves it with the formation of acetyl derivatives of ethyl *p*-diaminoterephthalate.

When the phenyluramino ester was boiled with a freshly prepared alcoholic solution of sodium ethylate, a yellow sodium salt separated, which was dissolved in water and the solution precipitated by adding acetic acid. This precipitate may be the free phenyluramino acid

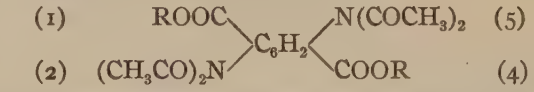


but not enough was obtained for an analysis.

By heating the phenyluramino ester with a fifty per cent. solution of hydrazine hydrate in a sealed tube for four hours at 130°, a yellow amorphous substance was obtained not melting below 320°, insoluble or very difficultly soluble in water or alcohol, and unchanged by six hours boiling with acetic anhydride. It dissolved in dilute caustic alkali, and was reprecipitated from such solutions by acids. It has not been further studied.

When the phenyluramino ester is heated with aniline a naphthotetrazine is formed as described beyond.

Ethyl Tetracetyl-p-diaminoterephthalate,

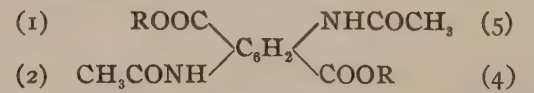


The above phenyluramino ester was boiled for about four hours with an excess of acetic anhydride in a flask with a return condenser, when a clear, almost colorless, solution resulted. This solution was concentrated until crystals began to appear, when it was allowed to cool and the tetracetyl derivative crystallized out. During the concentration the solution darkened somewhat. The crude product was purified by recrystallization from alcohol, and gave the following figures on analysis:

Found: C, 57.16 and 57.61; H, 5.83; N, 6.73. Calc. for $C_{20}H_{24}O_8N_2$: C, 57.14; H, 5.71; N, 6.66.

The by-products were acetanilide and carbon dioxide. The pure substance forms colorless crystals, melting at 207-208° (corr.), apparently insoluble in water, but soluble in alcohol or benzene without fluorescence.

Ethyl s-diacetyl-p-diaminoterephthalate,



An excess of alcohol was added to the mother-liquor from the above tetracetyl derivative, and the solution boiled. On cooling, the diacetyl derivative separated in large crystals. These were purified by recrystallization from alcohol and bone-blacking, and the product analyzed.

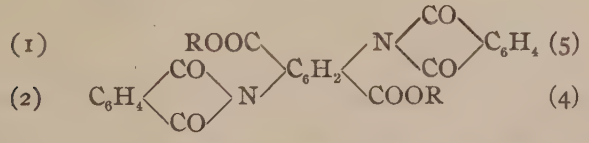
Found: C, 57.07 and 57.48; H, 5.83 and 5.97; N, 8.50. Calc. for $C_{16}H_{20}O_6N_2$: C, 57.4; H, 5.95; N, 8.33.

The pure compound is yellowish white, with a decided greenish fluorescence, while the corresponding tetracetyl derivative is colorless and shows no trace of fluorescence. It melts at 219° (corr.) and is soluble in alcohol, benzene and most of the ordinary organic solvents.

When acetic anhydride was added to ethyl *p*-diaminoterephthalate itself, heat was evolved and the ester gradually went into solution. This solution was evaporated until crystals began to form (the color of the solution darkening somewhat during the concentration), and was then allowed to cool. The crystalline mass which separated was purified as before, and yielded the diacetyl derivative identical with that obtained from the phenyluramino ester. The formation of the tetracetyl diaminoterephthalate was not, however, observed. Boiling the diacetyl compound with phenylhydrazine or with benzylamine caused no change, but when it was heated with propylene diamine in a sealed tube for six hours at 150°, large yellow crystals separated on cooling. These have not been further examined.

The diacetyl derivative was also obtained by heating the ethyl diamino ester with acetyl chloride in presence of calcium carbonate.

Ethyl p-diphthalimidoterephthalate,



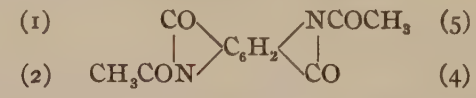
Ethyl *p*-diaminoterephthalate was fused with an excess of phthalic anhydride, and the claret-colored melt when cold extracted repeatedly with boiling alcohol. There remained a cream-colored crystalline residue, which softened slightly at 320° and melted at 326° (corrected). It is moderately soluble in hot benzene, difficultly soluble in toluene, and very difficultly soluble in chloroform.

Found: N, 5.70. Calc. for $C_{28}H_{20}O_8N_4$: N, 5.47.

This compound was heated with aqueous ammonia in a sealed tube for four hours at 150°; a dark brown solution was formed. This was evaporated to dryness on the water bath, and left a dark brown hydroscopic mass. When the latter was carefully heated, a white crystalline sublimate collected. M. p. 228° (uncorr.), but not enough material was obtained for an analysis.

Ethyl diiminosuccinylosuccinate was treated with phthalic anhydride in a similar way, but so much decomposition took place that no product could be isolated. Same results were also obtained when ethyl succinylosuccinate and phthalimide were fused together.

Di-lactam of p-Diacetyldiaminoterephthalic Acid,



In the course of some experiments on the reduction of the benzene nucleus, an alcoholic solution of ethyl diacetyl-*p*-diaminoterephthalate was treated with sodium amalgam upon the water-bath. Instead of reduction, however, saponification occurred, and a sodium salt separated as a white precipitate. This was dissolved in water and the free acid precipitated by the addition of dilute acetic acid. The product was white, infusible, and insoluble in ordinary organic solvents. Judging by its color and other properties, it may have been the diacetyl-*p*-diaminoterephthalic acid, for the free diaminoterephthalic acid is yellowish green. This point will be cleared up later. On boiling the compound with acetic anhydride, it slowly dissolved, and on cooling, white infusible flakes separated, which were purified with difficulty. The analysis gave the following figures:

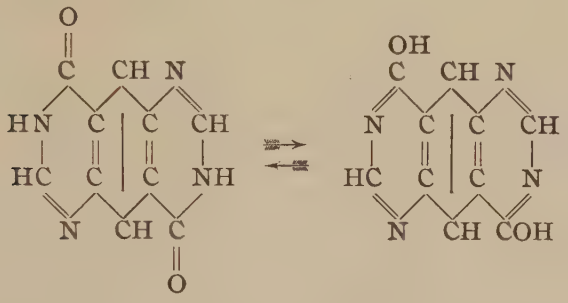
Found: N, 11.07. Calc. for $C_{12}H_8O_4N_2$: N, 11.47.

Bogert and Dox[9] reported *p*-diaminoterephthalic acid unchanged by boiling acetic anhydride. It was found that when diaminoterephthalic acid is boiled with acetic anhydride, it gradually dissolves, and on cooling the same di-lactam crystallizes out as mentioned above, except the crude product thus obtained is apt to be rather darker in color.

[9] See 2.

Found: N, 11.50. Calc. for $C_{12}H_8O_4N_2$: N, 11.47. (For convenience, this di-lactam is called "diacetanthranil") in the experiments which follow.

4,9-Diketotetrahydro-1,3,6,8-naphthotetrazine (*4,9-Dihydroxy-1,3,6,8-naphthotetrazine*),



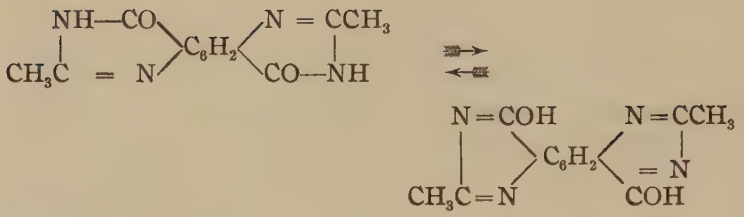
NOTE.—This numbering of the nucleus is that adopted in Richter's "Lexikon."

Seven grams of ethyl *p*-diaminoterephthalate and ten grams formamide were heated together in a sealed tube for seven hours at 200-210°. An excess of formamide was used in order that it might act also as a solvent. At the close of the reaction, the tube was filled with a gray crystalline mass, which was purified by dissolving in dilute potassium hydroxide solution and reprecipitating with carbon dioxide. When thus purified, it appeared as an amorphous pale yellow powder. The yield was theoretical.

Found: C, 55.91; H, 3.21; N, 26.20 and 25.94. Calc. for $C_{10}H_6O_2N_4$: C, 56.07; H, 2.8; N, 26.17.

The substance melts above 310°. It is insoluble, or very difficultly soluble in water, alcohol, benzene, or the usual neutral organic solvents. It evidently dissolves in formamide at high temperatures, for the crystals which separated in the tube were large and well formed, as well as being practically pure. It dissolves readily in dilute caustic alkalies and is reprecipitated from such solutions by dilute acids or carbon dioxide.

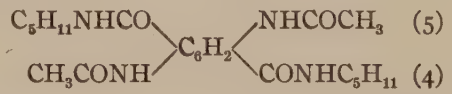
2,7-Dimethyl-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine (*2,7-Dimethyl-4,9-dihydroxy-1,3,6,8-naphthotetrazine*),



Ethyl diacetyl-*p*-diaminoterephthalate was heated with excess of alcoholic ammonia in a sealed tube for five hours at 200°. When cold, the tube contained a mass of greenish crystals. These were dissolved in dilute potassium hydroxide solution and precipitated by carbon dioxide. The precipitate was washed with hot water, and dried at 110°, and analyzed: Found: N, 22.47. Calc. for $C_{12}H_{10}O_2N_4$: N, 23.1. Considerable difficulty was encountered in purifying this substance. When precipitated by carbon dioxide from alkaline solution, it separated as a mud, which was not easy to wash thoroughly, and the figure for nitrogen is therefore too low.

The dry substance is a pale yellow, amorphous powder, with a greenish cast, which melts above 325°.

Diacetyl-p-diaminoterephthalisoamylamide,

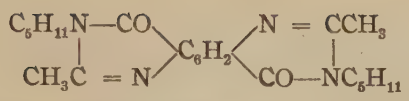


Ethyl diacetyl-*p*-diaminoterephthalate was heated with isoamylamine. A clear solution was obtained, which deposited a white substance on cooling. This was recrystallized from dilute alcohol, and analyzed:

Found: N, 13.84. Calc. for $C_{22}H_{34}O_4N_4$: N, 13.4.

The pure compound forms long, colorless, silky needles, which soften at 246° (corr.) and melt at approximately 255° (corr.) apparently with partial conversion to the naphthotetrazine. The substance is insoluble in water, but dissolves in alcohol, benzene and other organic solvents. Caustic alkalies change it to the corresponding naphthotetrazine. This same amide was obtained also from the diacetanthranil and isoamylamine.

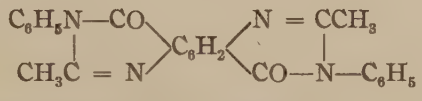
2,7-Dimethyl-3,8-diisoamyl-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine,



When the above isoamyl amide was boiled for ten or fifteen minutes with dilute potassium hydroxide solution, it changed considerably in appearance. On filtering out the product and recrystallizing it from alcohol, yellowish white needles, with greenish flourescence, were obtained, melting at 179° (corr.).

Found: N, 14.64. Calc. for $C_{22}H_{30}O_2N_4$: N, 14.66. Brominated in acetic anhydride solution, this tetrazine gave a yellowish white crystalline bromine derivative, melting in the neighborhood of 290°.

2,7-Dimethyl-3,8-diphenyl-4,9-diketotetrahydro-1,3,6,8-naphthotetrazine,

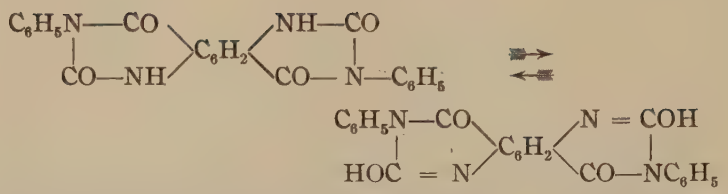


Ethyl diacetyl-*p*-diaminoterephthalate and aniline were heated together at ordinary pressure and for two hours at 180° in a sealed tube, but no change was observed in either case. But when the diacetanthranil was heated for fifteen minutes with aniline, small yellow crystals separated from the solution on cooling. These were recrystallized from acetic anhydride, washed with alcohol and dried; or, the crude product was easily purified by washing with boiling acetic acid and then boiling alcohol.

Found: N, 14.29. Calc. for $C_{24}H_{18}O_2N_4$: N, 14.21.

This is evidently the diphenylnaphthotetrazine sought, as the percentage of nitrogen in the corresponding amide is only 13.02. The pure substance crystallizes in greenish yellow leaflets, which are unmelted at 325°. The compound is insoluble in alcohol or acetic acid, and very difficultly soluble in hot nitrobenzene.

3,8-Diphenyl-2,4,7,9-tetraketo-octahydro-1,3,6,8-naphthotetrazine (3,8-Diphenyl-2,7-dihydroxy-4,9-diketotetrahydro-1,3,6,8,-naphthotetrazine),

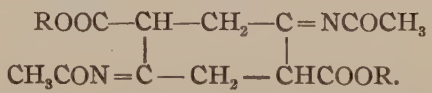


Ethyl diphenyluraminoterephthalate was heated with aniline in a sealed tube at 225° for six hours. Considerable decomposition was evident in the tube. By boiling the product with glacial acetic acid, the tarry impurities were removed, leaving a bright yellow crystalline residue.

Found: N, 13.99. Calc. for $C_{22}H_{14}O_4N_4$: N, 14.07.

The phenyluramino ester and aniline were also boiled together in an open test-tube, but no reaction occurred. The purified substance is yellow and crystalline and does not melt below 330°. It is apparently insoluble in water, alcohol, or glacial acetic acid. In dilute caustic alkalies it dissolves, and is reprecipitated from such solutions by acetic acid.

Ethyl Diacetyliminosuccinylosuccinate,



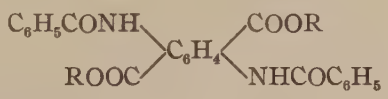
This substance is much less stable than the corresponding diacetyl-diaminoterephthalate, and its preparation is hence more difficult. It was obtained as follows: A very slight excess of acetic anhydride was added to ethyl diimino-succinylosuccinate and cause but little rise in temperature. The mixture was carefully warmed until a clear solution was obtained, which was then cooled. The excess of acetic anhydride was neutralized by ammonia, and any excess of ammonia carefully neutralized with acetic acid. The crystalline product was purified by recrystallization from dilute alcohol, washing the crystals occasionally with ether. The loss in purification was considerable, and the final yield poor. The purified substance forms fluffy, white crystals, with greenish fluorescence, which melt sharply at 215°-216° (corr.), and are easily soluble in alcohol or benzene, but difficultly soluble in ether.

Found: N, 8.35. Calc. for $C_{16}H_{20}O_6N_2$: N, 8.3.

This compound was dissolved in alcohol and boiled with sodium ethylate, thereby causing the general separation of a white sodium salt. This salt was dissolved in water and acetic acid added. There resulted a white precipitate, apparently the free acid. It was very unstable and decomposed with evolution of carbon dioxide. This instability of the free acid is quite in line with the free succinylosuccinic acid itself. Not enough of the material was prepared for an analysis.

When calculated amount of acetyl chloride was added to the ester in presence of pyridine, considerable heat is produced, and a clear solution obtained. When water was added to this solution a yellow precipitate was thrown out. This, after bone-blacking in an alcoholic solution, was obtained from this solvent in fine yellowish white crystals with a greenish fluorescence, and melting at 215°. This product is therefore the same diacetyl-diiminosuccinylosuccinate as obtained by means of acetic anhydride and the ester.

Ethyl s-dibenzoyl-p-diiminosuccinylosuccinate,



Ten grams of the ester were added to 75 grams of pyridine and 11 cc. of benzoyl chloride added. When alcohol was added, after the reaction was over, a light yellow precipitate was obtained. This product was recrystallized from benzene in yellow feathery needles, melting at 255° (uncorr.).

Found: N, 6.62. Calc. for $C_{26}H_{26}O_6N_2$: N, 6.06.

The high nitrogen is very likely due to the difficulty of removing the last traces of pyridine.

The benzoyl derivative is soluble in acetic anhydride, and when bromine was added to this solution and warmed, upon cooling a finely powdered, heavy precipitate was obtained, melting at 264° (uncorr.) and probably is the *ethyl s-dibenzoyl-p-diaminoterephthalate.*

RESUMÉ.

(1) Ethyl *p*-diaminoterephthalate forms with phenylisocyanate, ethyl *p*-diphenyluraminoterephthalate.

(2) Ethyl *p*-diphenyluraminoterephthalate is decomposed by acetic anhydride into the tetra and diacetyl derivatives of ethyl *p*-diaminoterephthalate.

(3) Ethyl *p*-diaminoterephthalate can be acylated by both mono and bibasic acid anhydrides.

(4) Ethyl diiminosuccinylosuccinate is more difficultly acylated, due to the less stability of this series.

(5) Ethyl diaminoterephthalate condenses with formamide yielding a naphthotetrazine.

(6) Ethyl diacetyldiaminoterephthalate condenses with primary amines to form naphthotetrazines or intermediate amides.

(7) Diacetanthranil condenses with primary amines more readily than the ester.

(8) Ethyl *p*-diphenyluraminoterephthalate condenses with primary amines, as aniline, to form the corresponding naphthotetrazines.

PART II.

ISOMERISM OF ETHYL DIIMINOSUCCINYLOSUCCINATE AND ETHYL *p*-DIAMINOTEREPHTHALATE.

Ethyl diiminosuccinylosuccinate, as prepared by Baeyer,[10] is a golden yellow compound. When an alcoholic solution of this substance is boiled in the presence of alkalies, it is changed into a colorless isomer. A change in color also takes place, although not as readily, when ethyl *p*-diaminoterephthalate, in an alcoholic solution is boiled with alkali salts of weak acids. Instead, however, of obtaining a colorless modification in this case, some of the yellow modification, first described by Häusermann and Martz[11] results in place of the usual red compound.

HISTORICAL PART.

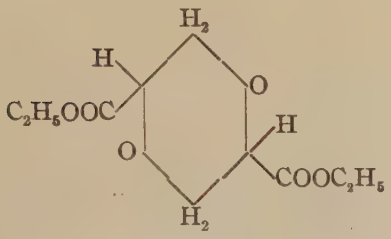
Baeyer[12] did not enter into the possible structure of ethyl diiminosuccinylosuccinate, at the time he worked out its mode of preparation, but concluded as a simple explanation for the

[10] Baeyer, Ber., **19**, 428 (1886).

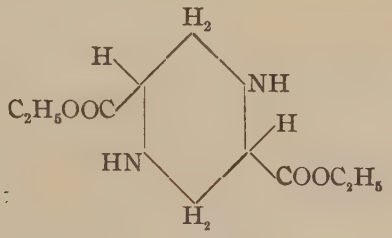
[11] Hausermann and Martz, Ber., **26**, 2984 (1893).

[12] See 10.

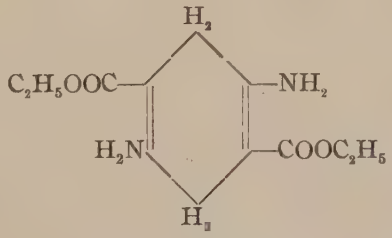
reaction, that two imino groups replaced the two oxygens in the keto groups of the ester.



$+ 2NH_3 =$



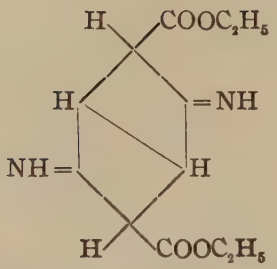
Geuther[13] believed that ethyl succinylosuccinate always acted as ethyl dioxydihydroterephthalate and that the diimino structure by Baeyer was incorrect, that it really was ethyl diaminodihydroterephthalate.



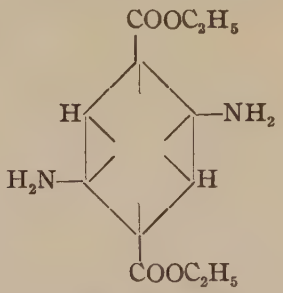
Hantzsch and Hermann[14] assigned to the red ethyl diaminoterephthalate the quinoid structure

[13] Geuther, Ann. der Chem., 244, 213 (1886).

[14] Hantzsch and Hermann, Ber., 21, 1755 (1888).

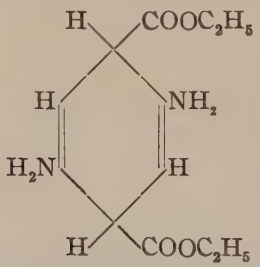


on account of its color. To its salts with strong mineral acids, all of which are colorless, the diamino structure.



The mineral acids inducing the change of the imino to the more basic amino group.

Muthmann[15] has shown that ethyl diimino-succinylosuccinate has two asymmetric carbon atoms. The only structure in which this can be the case is the $\Delta^{2,5}$ diamino structure.

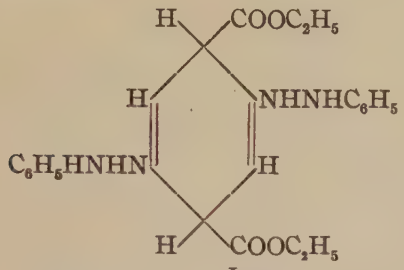


Baeyer and Brüning[16] have shown that phenylhydrazine gives with ethyl succinylosuccinate two isomeric ethyl benzol-

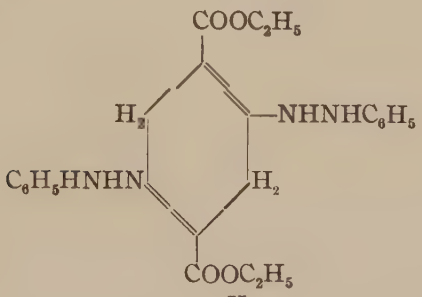
[15] Muthmann, Zeit. f. Kryst., 15, 60.

[16] Baeyer and Brüning, Ber., 24, 2692 (1891).

bisphenylhydrazinodihydroterephthalates, one white and the other yellow. To these two isomers they assigned the following structures:



I.
Colorless.



II.
Yellow.

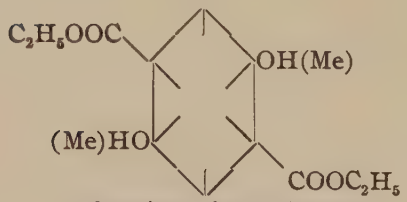
and were of the opinion that the difference in color was due to the position of the double bonds. From this they concluded that the true structure of ethyl diiminosuccinylosuccinate must be the diaminodihydroterephthalate, and that there was a possibility of a white form of this compound. These two forms would then correspond to the colorless and yellow forms of the phenylhydrazine derivatives, having —NH_2 groups in place of the —$NHNHC_6H_5$— groups.

Nef[17] stated that the isomerism occurring in ethyl succinylosuccinate and its derivatives was not desmotropic or tautomeric, as Hantzsch and Hermann had stated, but that it depended upon the position of the double bonds, and he called this a physical isomerism, for in no other way could the five

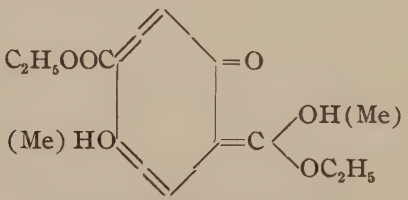
[17] Nef, Ann. der Chem., 258, 270 (1890).

benzoyl-dioxydihydroterephthalates prepared by him, be explained, and there succinylosuccinic ester always reacted in the enolic form, and thus the diamino structure should be correct in case of ethyl diiminosuccinylosuccinate.

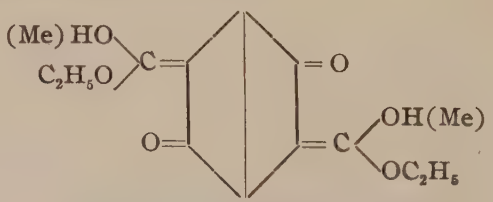
More recently, Eyre[18] and Hantzsch[19] have bought out a rearrangement theory for the explanation of difference in color exhibited by salts of compounds like ethyl dioxyterephthalate. The rearrangement is due to the labile hydrogens, giving rise to quinonehydro and hydroquinone structures,



Hydroquinone form colorless.



Quinonehydro slightly colored.

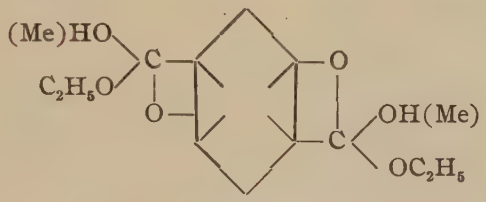


Double quinonehydro highly colored.

Since then Hantzsch[20] has proposed a peroxide structure in place of the above quinonehydro, for the colored modifications, because of the existence of compounds which yield colored derivatives, and do not contain the benzene nucleus, and

[18] Eyre, Diss., Leipzig (1905).
[19] Hantzsch, Ber., 39, 3098 (1906).
[20] Hantzsch, Ber., 40, 335 (1907).

therefore no possibility of a quinone formation. This peroxide structure is represented by the following formula:



THEORETICAL PART.

In the following discussion I have retained the common name ethyl diiminosuccinylosuccinate for both forms of the isomers.

From the preceding historical part, five different theories suggest themselves for consideration, as to the probable structure of these isomers.

I. Extending the view of Hantzsch and Hermann in connection with ethyl *p*-diaminoterephthalate so that it will also include the isomeric forms of ethyl diiminosuccinylosuccinate.

II. That in the case of ethyl diiminosuccinylosuccinate, the isomerism being due to the bonds as suggested by Baeyer and Brüning and also Nef.

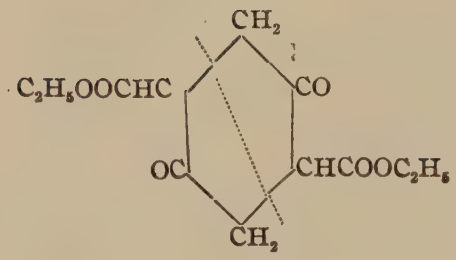
III. That the colorless and yellow forms of ethyl diiminosuccinylosuccinate are the cis and trans forms pointed out by Muthmann.

IV. That the isomerism in both ethyl diiminosuccinylosuccinate and ethyl diaminoterephthalate are due to migration of the labile hydrogen atom giving rise to quinonehydro and hydroquinone structures.

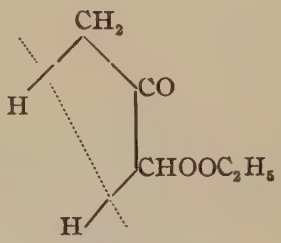
V. That instead of quinonehydro structure the peroxide formula be applied for the colored forms.

Theory (I) is very improbable, for even if it was the diimino form in case of the yellow ethyl diiminosuccinylosuccinate this would not be a true quinoid structure, but more like *p*-diketohexamethylene, which is colorless. It is also known that there are two *β*-aminocrotonic esters,[21] and since acetoacetic ester can be considered as semi-ethyl succinylosuccinate;

[21] Behrend, Ber., 32, 544.



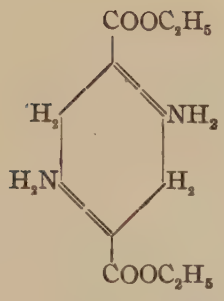
Ethyl succinylosuccinate.



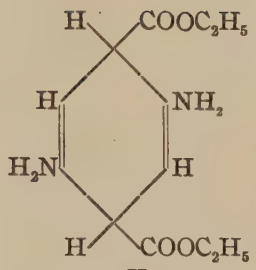
Acetoacetic ester.

and in the case of acetoacetic ester derivatives the possibility of quinone structure is excluded. (I) does not hold for the isomeric forms of ethyl diaminoterephthalate either, since if this was the case one of the isomers ought to be colorless.

Theory (II): There are many points of similarity between the two forms of benzolbisphenylhydrazinodihydroterephthalates and the two forms of ethyl diiminosuccinylosuccinate. The yellow forms in both cases are the more stable. The colorless forms are changed into the yellow forms by acids. In both series the two isomers are oxidized by means of bromine to the same terephthalic derivatives. One difference, however, is that when the yellow isomer of ethyl diiminosuccinylosuccinate is boiled in presence of alkalies, it is changed into the colorless modification, while the reverse is true in the two benzolbisphenylhydrazino compounds. Should this be the true explanation for the diimino derivatives, then they would have the following structures:



I.
Yellow form.



II.
Colorless form.

Nef[22] also succeeded in preparing five distinct isomers of benzoyl dioxydihydroterephthalate. These can only be explained by changing the positions of the double bonds, in which case there are six possible isomers. This is, of course, a strong point in favor of this theory in case of derivatives of succinylosuccinate.

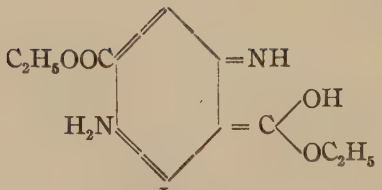
In theory (III), that ethyl diiminosuccinylosuccinate has two asymmetric carbon atoms, thus giving rise to cis and trans forms, is upheld by certain facts, such as the addition of traces of iodine to an alcoholic solution of the diimino compouud, changing the white form to the yellow. This is common to many cases of cis and trans compounds. For example, maleic acid is changed into fumaric in the same way.[23] When acetic acid is added to an alcoholic solution of the colorless ethyl diiminosuccinylosuccinate the yellow form is obtained; this is also the case in changing maleic to fumaric acid by means of hydrochloric acid.[24] No indication of cis and trans forms could be detected by means of the polariscope, in the two forms.

Theory (IV) is not applicable to the isomers of ethyl diiminosuccinylosuccinate, for similar reasons as in (I), but can be considered in the case of the two ethyl *p*-diaminoterephthalates, the two colored isomers being expressed by the following formulae, I and II:

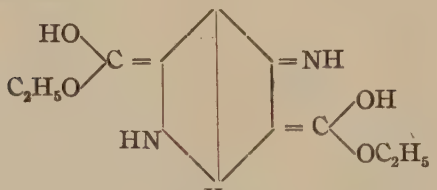
[22] See 17.

[23] Anschütz, Ber., 12, 2282.

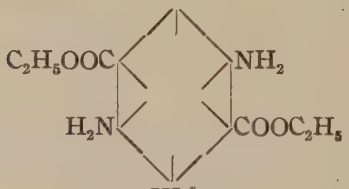
[24] Skraup, Monatsh. f. Chem., 12, 119.



I.
Yellow form.



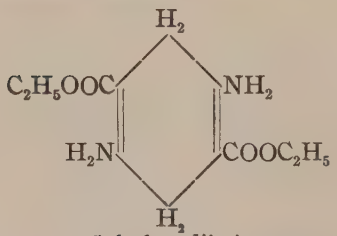
II.
Red form.



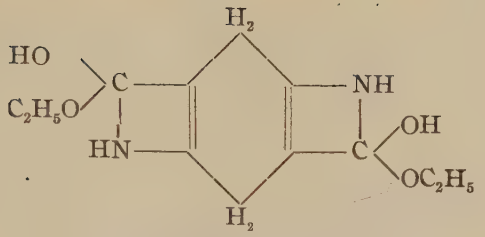
III.
Colorless form.

The tetracetyl diaminoterephthalate, described in Part I, is colorless, and therefore in accord with this theory, since it has no labile hydrogen atoms to rearrange into the colored forms I or II.

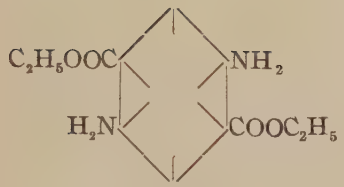
Theory V is the only one which seems to be applicable to both series, since this does not involve any quinoid structures. According to this idea, the following would correspond to the different isomers:



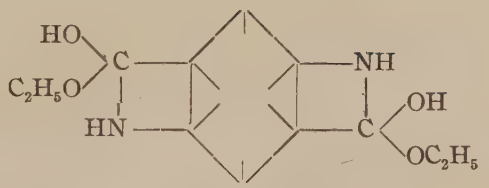
Colorless diimino ester.



Colored diimino ester.



Colorless forms.



Colored forms.

The point in favor of this theory is that it makes the isomerism in both series of a similar character, which is what one should expect, since the cause for the isomerism in both cases is apparently the same. Here we may look upon the two colored isomers of ethyl diaminoterephthalate as syn and ante forms of the peroxide type, just as Hantzsch has done in the case of the two differently colored alkali salts of nitrophenols[25]. One serious objection to all of the theories involving the migration labile hydrogen atoms is the fact that Nef[26] found that the methyl, ethyl and benzyl ethers of ethyl dioxyterephthalate were strongly fluorescent in their solutions. Here he points out that there is no possibility for labile hydrogens and still there is an indication of color, which should not

[25] See 20.

[26] See 17.

be the case, if Hantzsch's theory of labile hydrogens as the cause of color is correct. With this theory (V) the tetracetyl diaminoterephthalate coincides, just as in (IV).

One point which is noticeable about the color of the different derivatives of both ethyl diiminosuccinylosuccinate and ethyl *p*-diaminoterephthalate, is that as the basicity of the nitrogen in the amino groups is decreased the intensity of the color diminishes also. To illustrate this, the tetracetyl diaminoterephthalate, is colorless, and its solutions are also non-fluorescent. In this case both of the hydrogens in the amino groups have been replaced by acyl groups. Now in the case of the diacetyl diaminoterephthalate, in which only one of the hydrogens on each amino group is replaced by acyl groups, and therefore the nitrogen group being more basic, the compound is greenish white and the solutions show blue fluorescence, but the ethyl diaminoterephthalate itself, which would have nitrogen groups that are more basic than either of the acetyl derivatives, has still deeper color. The same results are also obtained in the case of the salts of ethyl diaminoterephthalate with strong acids, such as the sulphate and the hydrochloride. These are colorless, and in this case the nitrogen is also less basic than in the free base. The same seems to be the case with ethyl diiminosuccinylosuccinate, in regard to its diacetyl derivative which is greenish white in color, its mineral acid salts being practically colorless. Therefore, some experiments have been made to replace the hydrogens in the amino groups by alkyl groups, to see whether the color would become still stronger than that of the free amino compounds, since the nitrogen would be still more basic, or whether they behave like the acyl substituted amines, in which case this would lend further evidence to this theory (V). So far, however, no success has been met with, in replacing the hydrogens by alkyl groups, although several different methods have been tried.

EXPERIMENTAL PART.

The yellow ethyl diiminosuccinylosuccinate was prepared from ammonium acetate and ethyl succinylosuccinate, according to the method of Baeyer. From this, the colorless modification was obtained by boiling an alcoholic solution to

which a little aqueous solution of sodium hydroxide had been added. The boiling was allowed to continue for only a couple of minutes, when the alcoholic solution was poured into a beaker and allowed to cool. The colorless modification crystallized out in white needles, similar in shape to those of the yellow form. The two forms seem to have practically the same solubility in alcohol. The colorless form shows no fluorescence in its alcoholic solution. When a small amount of iodine is added, to this solution, it immediately turns yellow in color, and from this solution the yellow form crystallizes out. When a small amount of acetic acid is added to the alcoholic solution of the colorless product, the solution turns quickly, yellow, and the yellow crystals separate. Boiling an alcoholic solution of the colorless changes it to the yellow form. A few crystals of the yellow form were placed in a saturated solution of the colorless, and the colorless form separated out, showing that it was not merely a different crystalline form. The white crystals melt at 178° (corr.), the same point as the yellow. A mixture of the two also melts at 178°. It seemed at first as if the two might be the same substance after all, but by heating the colorless modification for a couple of hours at 150° in an air oven it gradually changed into the yellow form. This point was even more striking in the case of the two forms of ethyl *p*-diaminoterephthalate, which will be mentioned below. From this fact it seems that the white form is the less stable of the two, and that it changes into the yellow form before it reaches its melting point, and therefore they have the same melting point, it being really that of the yellow form. When the colorless form melted, it is changed into the yellow, and does not become colorless upon cooling. Both forms yield the same diacetyl-diiminosuccinylosuccinate when treated with acetic anhydride as described in Part I. Both forms are oxidized by bromine in a sulphuric acid solution, to diaminoterephthalate. The sulphuric acid solution of the yellow form is strongly fluorescent, while the same solution of the colorless form is not. Isonitrile tests were tried with both modifications, but no disagreeable odor was noticable in either case. Upon analysis the colorless

modification gave the same nitrogen value as calculated for the yellow.

Found: N, 11.18. Calc. for $C_{12}H_{18}O_4N_2$: N, 11.02.

It was also found that the yellow ethyl diiminosuccinylosuccinate could be easily changed into the colorless form by adding some formaldehyde bisulphite reagent to an alcoholic solution (containing about 20 per cent. water) of the yellow form and boiling this on the steam-bath for a few minutes, when most of the sodium bisulphite is thrown out of the solution, then decanting off the water-alcohol solution and allowing it to cool, when the colorless crystals were obtained just as in the case of using sodium hydroxide. The same results were obtained when sodium carbonate and methyl iodide were used in place of sodium hydroxide, but with either of these alone, as was also the case when sodium acid carbonate or sodium bisulphite was used, the crystals obtained were always straw colored, and it was therefore thought that this was very likely a mixture of the white and the yellow forms. Organic bases like pyridine seemed to have no effect in producing this change of the yellow to the colorless form. It was also noticed that the colorless crystals showed a strong tendency to resinify or darken when moist with their mother-liquor. A similar behavior occurs in the case of $\Delta^{1,5}$-dihydroterephthalic acid.[27]

Some ethyl *p*-diaminoterephthalate was dissolved in alcohol, and to this solution was added some sodium acetate. The solution was heated to boiling and then cooled rapidly, by surrounding the vessel with ice-water. The solution became much lighter in color, and a mixture of the yellow and red modifications of ethyl diaminoterephthalate was obtained. When these crystals were filtered from the mother-liquor on a suction funnel, a good deal of the yellow form changed to the red. When sodium carbonate was used in place of the sodium acetate, some of the yellow form was also obtained. The yellow crystals could be separated from the red by picking them out. They were flat needles, while those of the red variety are not flat. Both forms have the same melting point. The yellow form changes with great ease into the red when

[27] Baeyer, Ann. der Chem., 251, 257.

heated in an air oven to 100°. Also when the melting point was taken of the yellow variety, it could easily be noticed that it changed into the red form, when the temperature reached 110°. This explains, as mentioned before in the case of the two isomeric ethyl diiminosuccinylosuccinates, why the two varieties have the same melting point, since it is the melting point of the red and more stable variety.

ATTEMPTS TO PREPARE ETHYL DIALKYL DIAMINODIHYDRO-TEREPHTHALATE AND ETHYL DIALKYL-DIAMINOTEREPHTHALATE.

(1) Fusion of ethyl succinylosuccinate with dialkylamine acetates.

Diethyl amine acetate was prepared by adding slightly more than calculated amount of the amine to glacial acetic acid. This was then added to ethyl succinylosuccinate, in excess, and the mixture fused, just as in the case of ammonium acetate, but upon cooling the melt and dissolving out the excess of diethyl amine acetate with water, ethyl succinylosuccinate was obtained unchanged. The same results were obtained, when in place diethyl amine, diamyl amine, and dipropyl amine were used.

(2) The free secondary amines used in place of the acetates.

Diethyl amine and ethyl succinylosuccinate were heated in a test-tube, allowed to cool and twice out of five trials, a red colored product was obtained, which, after crystallizing from alcohol, melted roughly at 140°. Not enough of the substance could be obtained for an analysis, to see whether it was ethyl diethyldiaminodihydroterephthalate or not.

When diethyl amine is added to ethyl succinylosuccinate, considerable heat is evolved, and a salmon colored product is formed, which presumably is the diethyl amine salt. This is very unstable. When dried, it is decomposed, leaving as a residue ethyl succinylosuccinate.

Kuchert[28] obtained diethyl aminocrotonic ethyl ester by allowing a mixture of diethylamine and ethyl succinylosuccinate to stand for four weeks. Therefore diethyl amine and succinylosuccinate were mixed together, in a flask, and allowed

[28] Kuchert, Ber., 18, 619.

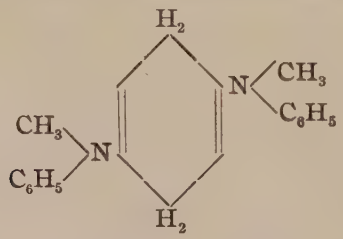
to stand for six weeks. The salmon colored product, which was formed as above, darkened slightly in color, and a strong odor of ammonia was noticeable, but when the product was removed from the flask and allowed to dry, ethyl succinylosuccinate was obtained.

Diamyl amine, dipropyl amine, and methyl aniline when heated in a test-tube with ethyl succinylosuccinate showed no signs of any condensation taking place.

Neither could any reaction be obtained when the ester was boiled with secondary amines in alcohol. In place of ethyl alcohol, amyl alcohol was also tried, because of its higher boiling point, and also since it is known that amyl alcohol favors the enolic condition of acetoacetic ester,[29] but no condensation was obtained.

(3) Heating in sealed tubes.

It was hoped that by heating the mixtures of the ester and secondary amines in sealed tubes to about 125° to 130°, that condensations could be effected, but in each case, the ester lost its carboxyl groups and oils were obtained. In case of methyl aniline, however, a product was isolated which proved by analysis to be *s-diphenyl-s-dimethyl dihydrophenylenediamine*



The heating was carried on at 200° for three hours. When the tube was opened, a great amount of carbon dioxide escaped, and the product after crystallizing from acetic acid was obtained in greenish yellow plates. No sharp melting point could be obtained even after several recrystallizations, the product always melting at 145 to 148°. The mother-liquor from these crystallizations had an intense blue color, which changed into a pink upon dilution with water.

Found: N, 9.83. Calc. for $C_{20}H_{22}N_2$: N, 9.65.

[29] Müller, Diss., Leipzig (1906).

From these experiments it was decided that condensations with secondary amines could not be carried out in sealed tubes, due to the ester being too unstable.

(4) It was hoped that by first making the diacetylsuccinylosuccinate, and then heating this with excess of secondary amines in a test-tube, that condensations might be obtained, but this was also unsuccessful.

(5) Dioxyterephthalic ethyl ester was next tried, in the hope that this would react with the secondary amines, but this method also proved unsuccessful.

(6) Ethyl diiminosuccinylosuccinate was dissolved in alcohol, and to this solution was added slightly more than the calculated amounts of sodium carbonate and methyl iodide, but no methylation took place, the ester being converted into the colorless modification.

(7) Experiments were also conducted, in which it was tried to methylate ethyl *p*-diaminoterephthalate by means of methyl iodide in an alcoholic solution, in the presence of such bases as sodium carbonate, silver oxide, metallic silver, and calcium carbonate; but none of the results obtained were of very much promise. When sodium carbonate was used, it gradually saponified the ester. Silver oxide oxidized the ester to a black tarry mass. Metallic silver had practically no effect, the hydriodic acid formed uniting with the amino groups of the ester instead. When methyl iodide alone was used, a hydriodide was obtained just as when metallic silver was employed. When ammonia was added to the hydriodide of the ester, the free ester was formed. This had a brilliant red color, but it seemed improbable that this deep red color was due to alkylation of the amino groups, since after repeated crystallizations from alcohol a product was obtained having a color very much like the orange-red color of the ester, and upon acetylation, by boiling with acetic anhydride it gave an acetyl derivative of the same nitrogen value as that calculated for ethyl diacetyldiaminoterephthalate, and also had the same melting point 219°. The only difference was that it was more yellow in color and deeper green fluorescent than ethyl diacetyldiaminoterephthalate, but this was very likely due to traces of impurities which were very hard to remove.

Thus no satisfactory method was found for alkylating the amino groups, since the amino groups are so strongly basic, that a strong base is necessary to prevent the hydriodide of the ester from forming, and when a strong enough base for this purpose is used, it saponifies the ester also.

RESUMÉ.

1. The yellow ethyl diiminosuccinylosuccinate can be changed into a colorless isomeric form by boiling its alcoholic solution in presence of alkalies.

2. The red ethyl diaminoterephthalate can be changed into a yellow isomeric form upon boiling its alcoholic solution with an alkali salt of a weak acid.

3. The less stable forms of the isomers in both ethyl diiminosuccinylosuccinate and ethyl diaminoterephthalate are changed into the more stable forms by heating below their melting points.

4. The isomerism in both cases seems to be of similar character.

5. So far the true structure of ethyl diiminosuccinylosuccinate and ethyl *p*-diaminoterephthalate and their isomeric forms have not been fully established.

PART III.

A DOUBLE INDIGO (β,β-BENZODIPYRROLIDINONE).

Ethyl *p*-diaminoterephthalate can be considered as a double anthranilic ester, and since the latter affords a means for synthesizing indigo[30] it seemed well to see whether a corresponding indigo could be prepared from the above ester. Several different plans were tried for the preparation of ethyl *p*-diglycine-terephthalate:

1. The condensation of ethyl *p*-diaminoterephthalate with chloracetic acid.

2. The condensation of the same compound with chloracetic ester.

3. By first preparing the ethylω-dicyan-dimethyl-*p*-diaminoterephthalate by means of formaldehyde bisulphite and potas-

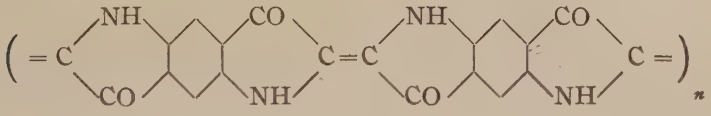
[30] Heumann, Ber., 23, 3431.

sium cyanide, then hydrolyzing this to *p*-diglycine-terephthalic acid, and converting the latter into the corresponding indigo by the usual methods employed in the preparation of indigo from *o*-carboxylphenyglycine by fusion with alkali.

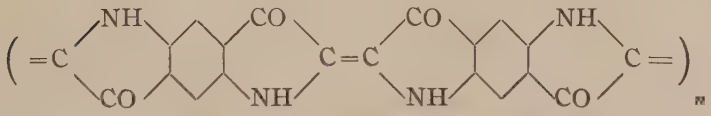
Furthermore, since phenylglycine has also been used in the preparation of indigo,[31] *p*-phenylenediamine was converted into the nitril of *p*-phenylenediglycine, and this hydrolyzed and fused with alkali.

All of these attempts met with no success as far as obtaining the double indigo was concerned, but in method (3), β,β-diacetylbenzodipyrrolol and ethyl ω-disodium sulphonate dimethyl-*p*-diaminoterephthalate were isolated as intermediate products.

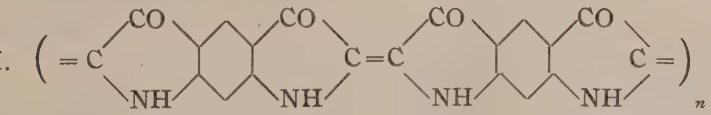
The failure to obtain the doube indigo by any of these proposed methods was thought to be due to some stereo-relations of the β-pyrrolinone groups, since these would alternatingly be inverted as can be seen from the following formulae:

I. 

or

II. 

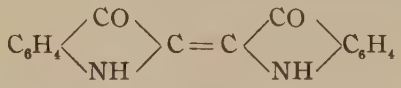
If this is the case, then *m*-phenylenediglycine should yield a double indigo, in which this stereo interference would not occur, as shown by its formula

III. 

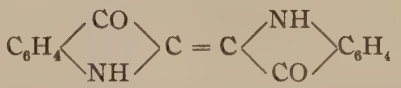
[31] Heumann, Ber., 23, 3044.

m-Phenylenediglycine was fused with potassium hydroxide, and a product obtained which showed many properties similar to those of indigo itself, as, for example, color, reduction to a colorless compound, and easy reoxidation.

As far as I know, no evidence has been put forth in the literature, why indigo is given the moleinoid structure

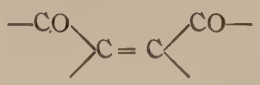


instead of the fumaroid structure



Baeyer[32] states that the deep blue color of indigo is due to the mutual intensification of the two indogen groups, and that the indogenides can be looked upon as similar to azo-compounds. He deos not, however, make any reference to the stereo relations of the indogens.

Friedlaender[33] believes that the —NH— groups in indigo only act as auxochromes, and that the real cause for the color is in accord with the color properties of unsaturated diketones and quinones containing the group



EXPERIMENTAL PART.

Ethyl p-diaminoterephthalate and chloracetic acid:

2.5 grams of ethyl *p*-diaminoterephthalate and 50 grams of chloracetic acid were heated to boiling in a flask on the sand bath. The solution gradually darkened, and hydrochloric acid was given off, which, after several hours boiling, exceeded the amount calculated for the ester used many times. The ester suffered a great deal of decomposition during the treatment, and a tarry product was obtained from which nothing definite could be isolated.

[32] Baeyer, Ber., 16, 2188 (1883).

[33] Friedlaender, Ann. der Chem., 351, 394.

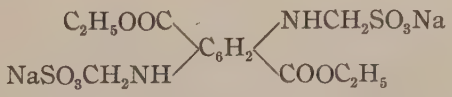
Ethyl p-diaminoterephthalate and chloracetic acid:

2 grams of the ester, 1.1 grams of sodium ethylate, and 1.9 grams of chloracetic ester (calculated amounts) were dissolved in 36 cc. of alsolute alcohol and boiled under a reflux condenser. Sodium chloride separated in large amounts. After twenty minutes boiling, the solution was practically neutral to litmus, and it was allowed to cool, when practically all the ester crystallized out unchanged.

Since no condensation was obtained in this way, the conditions were altered by taking calculated amounts of the ester, chloracetic ester and quinoline, and heating the mixture in a sealed tube for five hours at 200°. When the tube was opened, it was found that a large amount of carbon dioxide had been formed, showing that the ester had lost its carboxyl groups. The reaction product remaining in the tube was a dark tarry liquid, which was discarded.

Ethyl p-diaminoterephthalate, formaldehyde bisulphite and potassium cyanide:

5 grams of the ester, slight excess of formaldehyde bisulphite reagent (prepared as described by Koevenagel)[34] and 200 cc. of water were heated on a water-bath at 90° with constant stirring. After the lapse of about three hours all of the ester had gone into solution. This was then concentrated to about 75 cc. by boiling upon a sand-bath, allowed to cool, 50 cc. of alcohol added and allowed to stand over night. A bronze colored crystalline product separated out in clusters. This was filtered from the mother-liquor, washed with alcohol, and dried at 100°. It had no melting point, was readily soluble in water with a greenish fluorescence, and insoluble in all organic solvents tried. Upon analysis it gave a nitrogen value corresponding to *ethyl ω-disodium sulphonate dimethyl-p-diaminoterephthalate,*



Found: N, 5.87. Calc. for $C_{14}H_{18}O_{10}N_2S_2Na_2$: N, 5.78

Further attempts were made to prepare this sodium sulpho-

[34] Koevenagel, Ber., **37**, 4081.

nate derivative, in order to make certain that it was a definite compound, and also for its use in the preparation of ethyl *p*-diglycineterephthalate. In each case, although care was taken to duplicate the same conditions, as nearly as possible, that were previously employed, no bronze colored salt was obtained, but always a golden yellow colored salt of similar crystalline habit, and some general properties as the bronze, except in color. Upon analysis this golden yellow salt always gave a lower nitrogen value.

Found: N, 3.56. Calc. for $C_{14}H_{18}O_{10}N_2S_2Na_2$: N, 5.78.

By three recrystallizations from water.

Found: N, 4.28.

According to these nitrogen determinations the golden yellow salt is probably a mixture of ethyl ω-disodium sulphonate dimethyl-*p*-diaminoterephthalate and acid sodium sulphate.

The reactions taking place in the formation of the sodium salt might be represented by the following equation:

$$C_6H_2\left(\begin{matrix}NH_2\\COOC_2H_5\end{matrix}\right)_2 + 2CH_2\begin{matrix}OH\\SO_3Na\end{matrix} = C_6H_2\left(\begin{matrix}NHCH_2SO_3Na\\COOC_2H_5\end{matrix}\right)_2 + 2H_2O$$

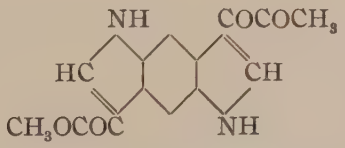
Since so much difficulty was experienced in trying to prepare the disodium sulphonate derivative, it was hoped that by adding potassium cyanide to the reaction mixture of the ethyl *p*-diaminoterephthalate and formaldehyde bisulphite, that the ethyl ω-dicyan-dimethyl-*p*-diaminoterephthalate could be isolated.

2.5 grams of the ester (0.01 mol), 6 cc. of aldehyde bisulphite reagent (0.02 mol + slight excess), 2 grams of potassium cyanide (0.02 mol and slight excess), and 200 cc. of water were heated on the water-bath with constant stirring for 15 hours, when the reaction mixture had formed a clear amber colored solution. No indication of the formation of the ω-cyan-dimethyl derivative could be noticed, but during the course of the reaction a fairly strong odor of hydrocyanic acid was noticeable, for which reason it seemed probable that the potassium cyanide was

partially hydrolyzed, and the alkaline solution formed saponified the ester, thus preventing the separation of ethyl ω-dicyandimethyl-*p*-diaminoterephthalate. To the amber colored liquid, some dilute potassium hydroxide was added and the solution boiled until ammonia ceased to be given off. Then upon cooling, dilute acetic acid was added, and a yellow flocculent precipitate was obtained. This was filtered off, but due to its gelatinous nature, it was impossible to wash it and obtain it pure enough for analysis. It is very difficultly soluble in water, alcohol, amyl alcohol or acetic acid, but readily soluble in alkalies, and strong mineral acids. Due to its insolubility in all the organic solvents tried, this way offered no means of its purification. Since *o*-carboxyphenylglycine yields, when treated with acetic anhydride, diacetylindoxyl[35] if this product is *p*-diglycineterephthalate it ought to behave similarly. The yellow product obtained above was heated to boiling with acetic anhydride when it gradually went into solution. Upon cooling, large brownish white flakes crystallized out. These were recrystallized from acetic anhydride, washed with carbon tetrachloride to remove the last traces of the anhydride, and analyzed.

Found: N, I, 10.55 and II, 10.12.

From the nitrogen values obtained, this product was concluded to be β,β-diacetyl-benzo-dipyrrolol, each pyrrolol group having only one acetyl group, instead of two as in the case of indoxyl, when treated the same way, and hence the following formula:



This has a calculated nitrogen content of 10.29 per cent.

The reactions involved in the various steps leading from ethyl *p*-diaminoterephthalate to the diacetyl derivative, have been represented by the following series of equations:

[35] C. Blatt (1900), II, 615.

1. $C_6H_2\left(\begin{matrix}NH_2\\COOC_2H_5\end{matrix}\right)_2+2CH_2\begin{matrix}OH\\SO_3Na\end{matrix}=$

$$C_6H_2\left(\begin{matrix}NHCH_2SO_3Na\\COOC_2H_5\end{matrix}\right)_2+2H_2O$$

2. $KCN+H_2O=HCN+KOH$

3. $C_6H_2\left(\begin{matrix}NHCH_2SO_3Na\\COOC_2H_5\end{matrix}\right)_2+2KOH=$

$$C_6H_2\left(\begin{matrix}NHCH_2SO_3Na\\COOK\end{matrix}\right)_2+2C_2H_5OH$$

4. $C_6H_2\left(\begin{matrix}NHCH_2SO_3Na\\COOK\end{matrix}\right)_2+2KCN=$

$$C_6H_2\left(\begin{matrix}NHCH_2CN\\COOK\end{matrix}\right)_2+2NaKSO_3$$

5. $C_6H_2\left(\begin{matrix}NHCH_2CN\\COOK\end{matrix}\right)_2+2KOH+2H_2O=$

$$C_6H_2\left(\begin{matrix}NHCH_2COOK\\COOK\end{matrix}\right)_2+2NH_3$$

6. $C_6H_2\left(\begin{matrix}NHCH_2COOK\\COOK\end{matrix}\right)_2+4HC_2H_3O_2=$

$$C_6H_2\left(\begin{matrix}NHCH_2COOH\\COOH\end{matrix}\right)_2+2KC_2H_3O_2$$

7. $C_6H_2\left(\begin{matrix}NHCH_2COOH\\COOH\end{matrix}\right)_2+2\begin{matrix}CH_3CO\\CH_3CO\end{matrix}\!\!>\!O=$

$$C_6H_2\left(\begin{matrix}NH\\\diagup\!\!\diagdown CH_2\\COOCCH_3\end{matrix}\right)_2+2CH_3COOH+2CO_2+H_2O$$

The β,β-diacetylbenzodipyrrolol is difficultly soluble in

strong, cold potassium hydroxide, which is also the case with diacetylindoxyl, and gradually turns red. When the potassium hydroxide solution is warmed the diacetyl compound dissolves, giving a light yellow solution. This last reaction might be due to the splitting open of the pyrrole rings with the formation of diaminoterephthalic acid, this being the case of indigo itself. When the diacetylbenzodipyrrolol was fused with solid potassium hydroxide at 260° in a long test-tube to exclude air as much as possible, and the melt allowed to cool, then dissolved in water, a red, difficultly soluble amorphous product was obtained, that showed no characteristics of an indigo.

Next an attempt was made to prepare the double indigo by starting with *p*-phenylenediamine.

11 grams *p*-phenylenediamine (0.1 mol), 50 cc. sodium bisulphite solution 34° Bé. (0.2 mols), 16 cc. 40 per cent. formaldehyde solution, and 20 cc. of water were placed in a flask and stirred continuously. Considerable heat was evolved in the reaction and after two minutes practically all the diamine had gone into solution. About ten minutes later shiny plates of the sodium salt of ω-disulphonic acid dimethyl-*p*-phenylenediamine commenced to separate. At this point 15 grams of potassium cyanide (0.2 mols and 2 grams excess) were added, and the stirring continued, when the plates of the sodium salt gradually changed into minutely crystalline grayish mass. After 12 hours the reaction was considered complete. Five times the original volume of water was added and the mixture allowed to stand for an hour and filtered. The gray crystals were dried upon a porous plate, and recrystallized from benzene in pinkish white plates, melting at 170° (corr.) The product is difficultly soluble in chloroform, insoluble in carbon tetrachloride, soluble in hot alcohol, hot benzene and hot water. Upon analysis found: N, 29.87 per cent. Calculated amount of nitrogen for *ω-dicyan-dimethyl-p-phenylene diamine*,

$$C_6H_4\begin{matrix}NHCH_2CN\ (1)\\ NHCH_2CN\ (4)\end{matrix} = C_{10}H_{10}N_4 \text{ is } 30.10 \text{ per cent.}$$

Since then there has come to my attention, a German patent,

(F 16,260)[36] in which the method given for the preparation of this compound and also the description of the properties of the product correspond closely with that stated above.

The ω-dicyan derivative was boiled with an alcoholic solution of potassium hydroxide in a flask provided with a reflux condenser. A strong evolution of ammonia was noticeable and a crystalline product separated which very likely is the potassium salt of *p*-phenylenediglycine. After the ammonia ceased to come off, the alcohol was evaporated, leaving the potassium salt together with the excess of potassium hydroxide. This was then dropped into molten potassium hydroxide and heated to 260°. During the heating, small portions of the melt were removed about every minute, allowed to cool, dissolved in water, and a current of air passed through the alkaline solution. In no case even after the fusion had been continued for about 20 minutes could any product be obtained which would give any blue coloration when air was passed through the alkaline solution, but instead a red, partially soluble amorphous product resulted. The red substance, when boiled in an alkaline solution with reducing agents, as glucose or zinc dust, gave no signs of reduction. It is improbable that this substance corresponds to indirubin, since the latter, too, is easily reduced to indirubin white.

To see whether any better results could be obtained, *m*-phenylene diglycine ester was prepared from *m*-phenylene diamine, according to the method of Zimmermann.[37] This was then fused with about three times its weight of potassium hydroxide at 260° until the melt ceased to froth, which required about 2 minutes. The melt was then allowed to cool and dissolved in water. Immediately a deep blue-green coloration developed, and when a current of air was passed through the alkaline solution a dark blue-green amorphous, difficultly soluble product was formed. This substance, when boiled in an alkaline solution with glucose, quickly loses its color, with the formation of an almost clear solution of a greenish yellow tinge. After repeating the oxidation with a current of air,

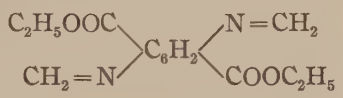
[36] Forts. f. Thier. Fabrik. Friedlaender, volume 1904-6.

[37] Zimmermann, Ber., 15, 518.

and then reducing with glucose again, it soon developed instead of the bluish green product, a red amorphous substance, very much like the product obtained in the case of the *p*-diamino series, showing that it is much less stable than indigo itself. If an alkaline solution of the above melt is poured upon a piece of cloth, the latter quickly assumes a deep bluish green color, but this color fades after several hours, finally assuming a dirty, greenish red. It therefore seems as though the position of the amino groups upon the benzene nucleus was of importance in determining the ease of formation of the double indigo.

Schiff Base of Ethyl p-Diaminoterephthalate.

A slight excess of formaldehyde bisulphite reagent was added to a hot, saturated alcoholic solution of the ester. The sodium bisulphite soon separated, while the aldehyde, as the boiling continued, turned the alcoholic solution a deep red. When this was filtered and allowed to cool, a deep red crystalline product was obtained. The crystals were minute needles. They were filtered from the alcoholic mother-liquor, recrystallized from alcohol, and gave a melting point of about 150°, although not sharp nor very constant. Upon analysis, they gave a nitrogen value corresponding to the Schiff Base.



Found: N, 10.05. Calc. for $C_{14}H_{16}O_4N_2$: N, 10.1.

A second preparation failed to give a value agreeing with this, and therefore the certainty of its being the Schiff Base requires further confirmation.

RESUMÉ.

The results obtained so far, although very imcomplete, tend to show:

1. Condensations between ethyl *p*-diaminoterephthalate and chloracetic acid or its ester do not take place very readily.

2. That the *p*-phenylene diamine derivatives, when fused with potassium hydroxide, do not give any compound ex-

hibiting properties similar to indigo, but a red substance which is not affected by reducing agents.

3. That *m*-phenylene diamine derivatives give a product when fused with potassium hydroxide that possesses the properties of an indigo.

4. That the bluish green product is less stable than indigo, changing into a red substance which is not affected by reducing agents.

5. The formation of an indigo-like substance from *m*-phenylene diamine derivatives and not from *p*-phenylene diamine derivatives, indicates that the malenoid structure is essential for the production of the blue chromophore group.

[1] Pinner, Ber., **22**, 2609 (1889).

[2] Bogert and Dox, J. Am. Chem. Soc., **27**, 1127.

[3] See 2.

[4] Meyer, Ann. der Chem., **347**, 17.

[5] Niementowski, J. prakt. Chem. [2], **51**, 564 (1895); Bogert and Chambers, J. Am. Chem. Soc., **27**, 650.

[6] Weddige, J. prakt. Chem. [2], **36**, 141 (1887); Zacharias, *Ibid.*, **43**, 432 (1891); Thieme, *Ibid.*, **43**, 451 (1891).

[7] Anschütz, Schmidt and Greiffenberg, Ber. **35**, 3480 (1902); Bogert and Chambers, J. Am. Chem. Soc., **27**, 649 (1905); Bogert and Seil, *Ibid.*, **27**, 1305 (1905); *Ibid.*, **28**, 884 (1906).

[8] Bogert and Dox, J. Am. Chem. Soc., **27**, 1136 (1905).

[9] See 2.

[10] Baeyer, Ber., **19**, 428 (1886).

[11] Hausermann and Martz, Ber., **26**, 2984 (1893).

[12] See 10.

[13] Geuther, Ann. der Chem., **244**, 213 (1886).

[14] Hantzsch and Hermann, Ber., **21**, 1755 (1888).

[15] Muthmann, Zeit. f. Kryst., **15**, 60.

[16] Baeyer and Brüning, Ber., **24**, 2692 (1891).

[17] Nef, Ann. der Chem., **258**, 270 (1890).

[18] Eyre, Diss., Leipzig (1905).

[19] Hantzsch, Ber., **39**, 3098 (1906).

[20] Hantzsch, Ber., **40**, 335 (1907).

[21] Behrend, Ber., **32**, 544.

[22] See 17.

[23] Anschütz, Ber., **12**, 2282.

[24] Skraup, Monatsh. f. Chem., **12**, 119.

[25] See 20.

[26] See 17.

[27] Baeyer, Ann. der Chem., **251**, 257.

[28] Kuchert, Ber., **18**, 619.

[29] Müller, Diss., Leipzig (1906).

[30] Heumann, Ber., **23**, 3431.

[31] Heumann, Ber., **23**, 3044.

[32] Baeyer, Ber., **16**, 2188 (1883).

[33] Friedlaender, Ann. der Chem., **351**, 394.

[34] Koevenagel, Ber., **37**, 4081.

[35] C. Blatt (1900), II, 615.

[36] Forts. f. Thier. Fabrik. Friedlaender, volume 1904-6.

[37] Zimmermann, Ber., **15**, 518.

BIOGRAPHICAL.

John Maurice Nelson entered the University of Nebraska in September, 1896, and graduated in June, 1901, receiving the degree of B.S. During the following two years he had the position as chemist for the Nebraska Pure Food Commission. In the fall of 1903, he went to Rose Polytechnic Institute as instructor in chemistry, which position he occupied for two years. While at this institution he published, together with Professor John White, a paper, "A Study of the Reactions Involved in the Formation of Certain Complex Salts of Lead," in the *American Chemical Journal*, **35**, 227. In 1905–6 he held a University scholarship in chemistry at Columbia University, and during this time and 1906–7 did research work in organic chemistry and studied for the degree of Ph.D. While at Columbia he published, together with Professor Marston T. Bogert, a paper on naphthotetrazines in the *Journal of the American Chemical Society*.